this method is capable of identifying novel polymorphisms as well as recognizing polymorphisms that have already been identified as informative for distinguishing the various alleles. When fully developed the method will be two-tiered i.e., capable of resolving KIR genotypes with locus-specificity or at an allele-specific level of resolution. We present data from previously characterized control DNA samples and transplant samples using this novel typing method to demonstrate that the method is capable of accurately defining KIR genotypes.

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REDUCED INTENSITY PERIPHERAL BLOOD STEM CELL TRANSPLANT FROM MATCHED RELATED AND UNRELATED DONORS FOR POOR RISK HEMATOLOGICAL MALIGNANCY

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46 patients with advanced, poor risk hematological malignancy underwent conditioning with Fludarabine 120 mg/m^2, Melphalan 140-180 mg/m^2 and Ethyol 910 mg/m^2 (FME) followed by peripheral blood stem cell transplant (PBSCT) from matched sibling (sib-allo) (n = 25) or matched unrelated donor (MUD) (n = 21). Average age was 46 years (range 19-65). Graft versus host disease (GVHD) prophylaxis consisted of mycophenolate mofetil 1 gram q12h through day 35 and dosage adjusted tacrolimus to a target trough serum level of 5-15 ng/ml through day 90. At 30 days (n = 46) transplant related mortality (TRM) was11%, overall survival (OS) was 89%, and relapse mortality (RM) was 0%. At 100 days (n = 45) TRM was 40%, OS was 51%, and RM was 9%. The most frequent causes of death at day 100 were acute GVHD, disease relapse, and adult respiratory distress syndrome. White blood cell engraftment was achieved in 98% of patients in an average of 13 days (range 9-21). This engraftment was achieved and maintained without the use of donor lymphocyte infusion (DLI). One patient died at day 24 without engrafment. Platelet engraftment was achieved in 80% of patients in an average of 18 days. In one patient the platelet count never declined below 20 k/μL. Eight patients died prior to platelet engraftment. All evaluable patients showed >95% donor marrow cells at 100 days after transplant. Acute GVHD incidence for patients not receiving DLI and alive more than 30 days after transplant was 56% (grade 2 = 1, 3 = 17, 4 = 4). For patients more than one year after transplant (n = 33) the OS was 30% (sib-allo = 37%, MUD = 21%) and disease free survival was 18% (sib-allo = 21%, MUD = 14%).

In this aged, heavily pretreated, poor risk group of patients, reduced intensity PBSCT using FME can yield short-term survival. This regimen provided rapid and durable engraftment with full donor hematopoiesis in a majority of patients without the need for DLI. In an effort to reduce the incidence of acute GVHD and hopefully TRM, we have added thymoglobulin to the conditioning regimen at 2 mg/kg/day to be given on days -2, -1, and 0. The impact on OS, DFS, and chronic GVHD remains to be determined.

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INTRAVENOUS BUSULFAN VERSUS MELPHALAN-BASED LOW INTENSITY CONDITIONING PRIOR TO ALLOGENEIC STEM-CELL TRANSPLANTATION: LOWER TRM AND A MORE FAVORABLE TOXICITY PROFILE

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Low intensity conditioning (LIC) regimens have been designed to reduce the toxicity associated with allogeneic stem-cell transplantation (SCT) and to allow SCT in elderly, heavily pretreated and medically infirm patients. However, the toxicity associated with some of these regimens is still substantial and it is currently unknown whether any of the regimens has advantage over the others. We compared the toxicity and 1-year treatment related mortality (TRM) following two LIC regimens: fludarabine and intravenous busulfan (FivBu) (total intravenous Busulfan dose 6.4 mg/kg) and fludarabine and melphalan (FM) (total melphalan dose, 100-140 mg/m^2). Fludarabine dose was 125-150 mg/m^2 in both regimens. Ninety-five patients with various hematologic malignancies (52% chemo-refractory) not eligible for standard conditioning, were included in the study. Forty-nine patients (52%) had a prior autologous SCT. The median age was 52 years (range, 20-66 years). Fifty-three patients had FM and 42 had FivBu. The donor was an HLA-matched sibling (n = 63) or a matched unrelated donor (n = 32). With a median follow-up of 10 months (range, 1-38) 55 patients are alive. Twenty patients (21%) have died due to TRM. TRM occurred in 4 patients (10%) and 16 patients (30%) within 1 year following FivBu and FM, respectively. The estimated Kaplan-Meyer TRM risk was 11 ± 5% and 33 ± 7%, respectively (p = 0.02). The univariant analysis also identified a prior autologous SCT within 1 year of the current SCT (p = 0.02) and diagnosis of lymphoma (p = 0.05) as risk factors for TRM. Age, donor source, and chemo-sensitivity were not significant. When these variables were included in a multivariable Cox regression model the hazard ratios for TRM for patients conditioned with FM, patients with a prior SCT and patients with lymphoma were 3.2 (1.1-9.6; p = 0.04), 2.5 (1.0-6.0; p = 0.05) and 2.2 (0.9-5.3; p = 0.08), respectively. Severe mucositis and organ dysfunction were more common after FM, while neutropenia duration was shorter after FivBu. In conclusion, FivBu has a more favorable toxicity profile and relatively low TRM as RIC for SCT and may prove to be the preferred LIC regimen. Disease-specific studies are required to assess the impact of different conditioning regimens on relapse rate, and whether reduction of TRM will translate to better disease-free survival.

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CYCLOPHOSPHAMIDE, TOTAL BODY IRRADIATION (TBI) AND MABCAMPATH (ALEMTUZUMAB) AS CONDITIONING FOR VOLUNTARY UNRELATED DONOR (VUD) HAEMOPOIETIC STEM CELL TRANSPLANTS (HSCT): THE SCOTTISH EXPERIENCE

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Scotland has a population of approximately 5 million people and supports a single VUD allograft centre based in Glasgow. We adopted a conditioning regime consisting of 60 mg/kg cyclophosphamide D-6 to D-5, TBI 1440 Gy in 8 fractions D-4 to 0 and Mabcampath 10 mg D-5 to -1 in year 2000. Data was collected retrospectively in 9/03 for the 21 VUD HSCT patients (pts) conditioned with this regime between 4/00 and 4/03. 11 males and 10 females were transplanted for the following diagnoses; 12 AML (7CR1, 5CR2), 4 ALL (2CR1, 2CR2), 4 MDS and 1 NHL (CR2). The median age was 31 years (range 17-50). Molecular tissue typing carried out at the A, B, Cw, DRB1 and DQ loci matched at all 10 loci in 17 pts. 3 pts mismatched at class 2 (2DRB1;1DQ) and 1 mismatched at 2 loci (DRB1 and Cw). 12 pts received unmodified bone marrow median dose 3.2x10^8 mononuclear cells/kg (range 1 to 6.7x 10^8) and 9 had peripheral blood stem cells median dose 7x10^6 CD34/kg (range 1.4 to 12x10^6). All received short course methotrexate and cyclosporine as graft versus host disease (GvHD) prophylaxis, which was tapered from D100 if there was no acute GvHD. Median follow up was 647 days (range 170 to 1233 days). The median time to neutrophil engraftment 0.5x10^9/l was 17 days (range 13 to 29 days) and platelets >20x 10^9/l was 17 days (range 11 to 32 days). There were no graft failures. Acute grade II-IV GvHD occurred in 5 pts (23.8%) with grade II in 3 (14.3%) and grade III in 2 (9.5%). No grade IV acute GVHD was seen. Of the 5 acute GvHD pts, 1 died of disease relapse, 2 died of post transplant lymphoproliferative disorder (PTLD), 1 developed chronic extensive GvHD (grade III pt) and 1 had complete resolution of acute GvHD. Relapse occurred in 5 pts (24%). The D100 transplant related mortality (TRM) was 14.3% and at 3.4 years the overall survival was 48% and TRM was 33%. There were 11 (52%) deaths in total, 4 due to disease relapse, 4 infection, 2 PTLD and 1 haemorrhage.

The incidence of grade II-IV acute GVHD is low supporting the use of Mabcampath as an effective anti-GvHD agent. The two cases of PTLD were surprising given that Mabcampath depletes